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Azole antimicrobial pharmacophore-based tetrazoles: Synthesis and biological evaluation as potential antimicrobial and anticonvulsant agents

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Abstract
The azole pharmacophore is still considered a viable lead structure for the synthesis of more efficacious and broad spectrum antimicrobial agents. Potential antibacterial and antifungal activities are encountered with some tetrazoles. Therefore, this study presents the synthesis and antimicrobial evaluation of a new series of substituted tetrazoles that are structurally related to the famous antimicrobial azole pharmacophore. A detailed discussion of the structural elucidation of some of the newly synthesized compounds is also described. Antimicrobial evaluation revealed that twenty compounds were able to display variable growth inhibitory effects on the tested Gram positive and Gram negative bacteria with special efficacy against the Gram positive strains. Meanwhile, six compounds exhibited moderate antifungal activity against Candida albicans and Aspergillus fumigatus. Structurally, the antibacterial activity was encountered with tetrazoles containing a phenyl substituent, while the obtained antifungal activity was confined to the benzyl variants. Compounds 16, 18, 24 and 27 were proved to be the most active antibacterial members within this study with a considerable broad spectrum against all the Gram positive and negative strains tested. A distinctive anti-Gram positive activity was displayed by compound 18 against Staphylococcus aureus that was equipotent to ampicillin (MIC 6.25 μg/mL). On the other hand, twelve compounds were selected to be screened for their preliminary anticonvulsant activity against subcutaneous metrazole (ScMet) and maximal electroshock (MES) induced seizures in mice. The results revealed that five compounds namely; 3, 5, 13, 21, and 24 were able to display noticeable anticonvulsant activity in both tests at 100 mg/kg dose level. Compounds 5 and 21 were proved to be the most active anticonvulsant members in this study with special high activity in the ScMet assay (% protection: 100% and 80%, respectively).

Author Keywords
1,3,4-Oxadiazoles; 1,3,4-Triazoles; 1H-Tetrazoles; Antibacterial activity; Anticonvulsant activity; Antifungal activity; Azoles; Pyrazoles

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